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Potassium Sorbate

I. BACKGROUND

Potassium sorbate has a long history of use as an antimicrobial food additive. Sorbic acid and its salts have broad-spectrum activity against yeasts and molds, but are less active against bacteria (1). The antimicrobial activity of sorbates is demonstrated below pH 6.5 and increases with the concentration of the undissociated acid as the pH of the medium is lowered (2).

Sorbic acid was isolated in 1859 from the berries of the mountain ash where it occurs as the lactone, parasorbic acid (2). There is no evidence that it occurs naturally either in tobacco or in mammalian species. Sorbic acid is now prepared commercially or by a number of synthetic procedures including: (a) the condensation of crotonaldehyde and ketene in the presence of boron trifluoride (3); (b) the condensation of crotonaldehyde and ketene in the presence of zinc isovalerate (4); and (c) the manganese catalyzed oxidation of 1,1,3,5-tetraethoxyhexane followed by the base catalyzed elimination of ethanol from the resulting 3,5-dimethoxyhexanoic acid (5). Potassium sorbate is prepared by the neutralization of sorbic acid with potassium hydroxide. The major US suppliers of potassium sorbate are Monsanto and American Hoechst Corporation.

Potassium sorbate is used as a preservative in a wide variety of foods such as cake mixes, carbonated beverages, fruit juices, wines, salads and fruit cocktails, dried fruits, margarine, canned fish products, jams and jellies, puddings, soft candy, and snack foods (1,2). It has recently been proposed that potassium sorbate be cleared for use in bacon, processed poultry, frankfurters and sausage (6). Production of potassium sorbate was 1.8 million pounds in 1970. More recent figures are not available; however, it is likely that food usage has increased since that time. Potassium sorbate is also used in the tobacco industry as a preservative. A representative level for potassium sorbate in tobacco is about 0.3 pounds per thousand pounds of tobacco. Therefore, some commercial cigarettes contain 0.23 mg potassium sorbate per cigarette.

The systematic chemical name for potassium sorbate is potassium trans, trans-2,4-hexadienoate. The salt is a white fluffy powder, highly soluble in water (58%) and slightly soluble in ethanol (6%). The melting point is 270°C with decomposition (7). Potassium sorbate is both tasteless and odorless (1). The specifications are set at not less than 98.0% and not more than the equivalent of 101% of $C_6H_7KO_2$ calculated on a dry weight basis by titration with 0.1N perchloric acid in glacial acetic acid using crystal violet as an indicator (8).

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II. REGULATORY STATUS

Potassium sorbate has generally recognized as safe (GRAS) status as both a chemical preservative for use in foods (FDA Code of Federal Regulations Section 182.3640) and for use on packing materials (FDA Code of Federal Regulations Section 182.90). In addition potassium sorbate has also been recognized as safe by the Flavor and Extract Manufacturers' Association (FEMA 2921) (1). As of 1972, seventeen countries in addition to the United States had approved sorbates for use as antimicrobial food additives including Canada, the United Kingdom, West Germany and Japan (1). With respect to tobacco usage, the United Kingdom has specified potassium sorbate by the Hunter List (<0.5% in cigarette tobacco), and the potassium salt of sorbic acid is mentioned on the German Tobacco Ordinance (<0.2% in tobacco sheet).

III. ACUTE AND CHRONIC TOXICITY

The oral LD_{50} of potassium sorbate in rats for the trans, trans-isomer was 4.9 g/kg. The ip LD_{50} value in mice was 1.3 g/kg (7). Rats administered a single dose of 200 mg of potassium sorbate had slightly elevated bilirubin, cholesterol, pancreatic juice, pancreatic protein, lipase and amylase, and decreased chymotrypsin activity (7).

Potassium sorbate was fed to groups of 10 rats (5 male and 5 female) at levels of 0, 1, 5, and 10% of the diet for three months. Relative liver weights were the same in all groups. Kidney weights were increased at the 10% and to a lesser degree at the 5% level. Weight gains of female animals were depressed initially when fed at the 10% level. Weight gains of female animals were depressed initially when fed at the 10% level and to a lesser degree at the 5% level. In the same report eight dogs received 1% and eight dogs 2% potassium sorbate in the diet for three months. The test animals gained the same weight as four control dogs. At autopsy, gross examination revealed no deleterious effects attributable to potassium sorbate (2).

Another three month feeding study was carried out using levels of 0.25% and 2% potassium sorbate in rats. At the 2% level, decreases in chymotrypsin, amylase and lipase were observed, while slight increases in bilirubin and cholesterol were noted. The only change noted at the 0.25% level was an increase in pancreatic juice, its protein content and all its enzymes (7). The general conclusion from these studies was that potassium sorbate poses no problem as an antimicrobial preservative with respect to either short term or long term toxicity.

The main metabolic products of sorbate in animals have been shown to be carbon dioxide and water. A small amount of trans, trans-muconic acid (0.1 - 0.2%) has been verified as a metabolic product in rabbits. The metabolism of sorbates is identical in animals and human beings (7).

IV. GENOTOXIC EFFECTS

Potassium sorbate has been found to be negative in chronic feeding studies with respect to carcinogenesis (7). In addition a number of studies have also shown potassium sorbate to be a non-mutagenic in a variety of bacterial test systems (see reference 6 and references cited therein).

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However some work has indicated a low level of genotoxic activity for potassium sorbate in a number of test systems.

A 1977 report demonstrated that potassium sorbate caused chromosomal aberrations in pseudo-diploid Chinese hamster cells, albeit only at the highest dose ($2x10^{2}M$). No sister chromatid exchanges (SCE) were observed at any dose. The authors point out that the dose at which chromosomal aberrations were noted was probably much higher than the doses taken in our daily lives (9).

A more thorough study of the potential genotoxicity of potassium sorbate as measured by chromosome aberrations and SCE was carried out by Hasegawa et al. (10). This study used V79 Chinese hamster cells. As in the Abe study (9), potassium sorbate was found to be clastogenic. However, chromosome aberrations were caused only at the highest dose (20 mg/ml), and about 50% of the clastogenic effect can be attributed to an increase in osmotic pressure. On the other hand, unlike the Abe study, potassium sorbate was found to cause a small but significant increase in SCE at a dose of 10 mg/ml. There was no dose response effect for the increase in SCE over the dose range 10 mg/ml to 20 mg/ml. This study also demonstrated that potassium sorbate was not mutagenic to V79 cells.

A report describing the mutagenic effects of the intestinal contents of mice fed both potassium sorbate and sorbic acid is of considerable interest. Mice were fed on a diet of 1.34%, 6.70% and 20.1% potassium sorbate for six months. The intestinal contents were removed from 5 to 10 mice from each group at one week and 1, 3 and 6 months, and ether extracts were tested for mutagenicity by the Ames assay using TA98 and TA100 plus and minus S9. No activity was detected in any of these samples (11). A group of animals fed on a diet consisting of 15% sorbic acid was tested similarly. Although the ether extracts were also negative in the Ames assay, the acid fraction from the ether extracts was weakly but significantly positive (11). Earlier results had shown that both potassium sorbate and sorbic acid were not mutagenic <u>per se</u> in the Ames assay using TA98 and TA100 plus and minus S9 (12).

In 1984 Tsuchiya and Yamaha published a follow-up (13) to their earlier study (11). In this case feeding was carried out for 12 months as compared to six months, and the acidic fraction of the ether extracts from all test groups were evaluated in the Ames assay. No mutagenicity of the acidic fractions of the ether extract of the intestinal contents of mice fed 1.34% and 6.70% potassium sorbate was detected. At the 20% potassium sorbate level, a slight mutagenic effect was observed, but only at the highest dose (8.0 mg/plate). However, there was a dose related depletion of liver glutathione levels for all doses tested.

One of the most interesting recent developments in the testing of potassium sorbate is the finding that mutagenic substances can be formed by the interaction of sorbate and nitrite at pH's which mimic gastric conditions. Two compounds have been isolated from this interaction which have been shown to be mutagenic; namely, ethylnitrolic acid and 1,4-dinitro-2-methylpyrrole. Formation of these compounds is blocked by ascorbate at low pH (6). On the other hand a recent report on the mutagenicity of sodium nitrite and potassium sorbate in combination indicates that mutagen formation may not occur under physiological conditions (14). Sodium nitrite was

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found to be cytotoxic to V79 cells, and a synergistic effect on cytoxicity was observed for sodium nitrite and potassium sorbate in combination. However, despite the fact that sodium nitrite alone was slightly mutagenic to V79 cells, the combination of sodium nitrite and potassium sorbate was inactive. It appears evident that the effects of nitrite and sorbate in combination need additional study before they can be said to be fully understood.

In the only study dealing with the potential genotoxicity of potassium sorbate on tobacco, the effect of adding potassium sorbate to cigarettes was evaluated by testing the resulting cigarette smoke condensate (CSC) in the Ames assay. Potassium sorbate was dissolved in water and injected into University of Kentucky 1R4F Research Cigarettes at levels of 1.5, 3.0 and 6.0 times those normally used in commercial cigarettes. The cigarettes were smoked, and the impaction-trapped CSC was tested in the Ames assay (strains TA98 and TA100) with and without metabolic activation. The results indicated that the addition of potassium sorbate to cigarettes, at any of the levels tested, did not alter the activity of the CSC.

Tests of potassium sorbate for teratogenicity by the chick embryo tests were negative. Daily administration of up to 460 mg/kg body weight to pregnant mice (albino CD-1) or up to 340 mg/kg body weight to pregnant rats (Wistar derived stock) for 10 consecutive days (day 6 to 15 of gestation) had no clearly discernable effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test group did not differ from the number occurring spontaneously in sham-treated controls (2).

V. PYROLYSIS DATA

The pyrolysis of potassium sorbate was investigated by performing Curie Point Pyrolysis/GC/MS at pyrolysis temperatures of 315°C and 590°C. No peaks were observed on the chromatograms at either pyrolysis temperature. These data indicate that potassium sorbate does not decompose to give any volatile products.

VI. REFERENCES

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